Remarks/Arguments

Prior to this amendment Claims 13-18 and 29-51 were pending. Claims 37, 38, 39 and 40 have been amended. Support is found throughout the specification as filed, for example at least at p. 8, lines10-11, and p. 12, lines 7-8. Applicants submit that no new matter is introduced by way of this amendment.

I. Rejection Under 35 USC § 102

A. Claims 40 and 44-47 are rejected under 35 USC § 102(e) as being anticipated by Ishikawa, et al. (U.S. 5,888,834). Applicants respectfully traverse. However, in an effort to expedite prosecution of this case, Applicants have amended the claims as set forth above.

It is well settled that an anticipatory prior art reference must teach " *all of the elements and limitations* contained in the claims." ATD Corp. v. Lydall, Inc., 159 F.3d 534, 545 (Fed. Cir. 1998). Here, Applicants respectfully submit that Ishikawa fails to teach all of the elements and limitations contained in the claims.

As amended, claim 40 is directed to a hybridization chamber that includes, *inter alia*, a lid comprising a plurality of second array components wherein a plurality of said second array components comprise a substrate comprising an array comprising discretes and comprising a plurality of different bioactive agents directly coupled to said discrete sites.

In contrast, Ishikawa discloses an immunoassay plate comprising a well and a dipstick. Attached to the dipstick is a substance (coating of a "receptor" for a functional group) for binding to the immune complex formed in the well. However, in contrast to the present claims, wherein a plurality of *different* bioactive agents are directly coupled to discrete sites on the substrate, Ishikawa only describes a single type of molecule attached to the dipstick, e.g. the receptor for the functional group that is coated on the dipstick. Moreover, the functional group receptor attached to the dipstick of Ishikawa is coated on the dipstick, not formed of discrete sites as required by the present claims. Thus, for at least the above reasons, Ishikawa fails to teach each element of the claims. That is, Ishikawa fails to disclose a plurality of *different* bioactive agents on the substrate. In addition, Ishikawa fails to describe any bioactive agents at discrete sites. Accordingly, Applicants respectfully request the Examiner to withdraw the rejection.

B. Claims 39-41 and 44-47 are rejected under 35 USC § 102(a) as being anticipated by Dunnington, et al. (WO 98/08092). The Examiner's position appears to be that the Dunnington, et al. reference teaches each element of the rejected claims. Applicants respectfully traverse. However, in an effort to expedite prosecution of this case, Applicants have amended the claims as set forth above.

As amended, claim 39 and 40 are directed to a hybridization chamber that includes, *inter alia*, a lid comprising a plurality of second array components wherein a plurality of said second

array components comprise a substrate comprising an array comprising discretes and comprising a plurality of different bioactive agents at said discrete sites. In claim 40, as noted above, a plurality of different bioactive agents are directly coupled to said discrete sites.

In contrast, Dunnington discloses a device that includes a capillary array. Each capillary of the array includes a single type of bead. However, there is no disclosure in Dunnington of a plurality of second array components that comprise a plurality of different bioactive agents as required in claim 39. Rather, Dunnington only describes compounds attached to the beads in the context of synthetic methods where the beads in each capillary are treated identically. In this regard Dunnington states on page 3, third paragraph:

> Synthesis of chemical compounds on bead arrays can be carried out using a similar procedure. The process for synthesis of pre-arrayed libraries according to the invention is carried out by arraying blank beads into capillaries. The capillaries containing the beads are dipped into multiwell containers, each well containing a different chemical reagent. Compounds are assembled on the beads by successive transfer of the capillary array into appropriate reagent plates.

Because the beads in each capillary are treated identically they will contain the same compounds. Absent description of the capillaries having a plurality of different bioactive agents, Dunnington fails to teach each element of the claims.

In addition, Applicants submit that there is no disclosure of a plurality of different bioactive agents directly coupled to second array components as required in claim 40. The Office Action appears to allege that capillaries 104 and 108 of Dunnington are second array

components as claimed. However, Applicants submit that Dunnington only describes the capillaries as having compounds attached to beads. Absent description of compounds coupled to the capillaries instead of the beads, Dunnington does not describe bioactive agents *directly* coupled to the second array as claimed.

Because each and every element of the claims is not present in either of the cited references, Applicants respectfully request the Examiner to withdraw the novelty rejections.

II. Rejection Under 35 USC § 103

A, Claims 13-18, 29-34 and 40-48 are rejected under 35 USC § 103(a) as being unpatentable over Whitehead, et al. (U.S. 4,879,097) in view of Kolehmainen, et al. (U.S. 4,349,510).

Whitehead discloses a device that includes a base plate for holding a microtiter plate. The device also includes a lid with ports for immobilizing components. The device includes a labyrinth joint between the base and the lid. The joint of Whitehead is, among other things, to prevent entry of stray light.

The Kolehmainen reference discloses an optical analysis system for detecting chemiluminescence. The reference discloses that a light-tight seal can be maintained using an O-ring.

In contrast, Claim 13 is directed to a hybridization chamber that includes a base plate with a cavity for holding a first array component formed in the base plate, a lid comprising at least one component port for immobilizing a second array component, and a sealant between the lid and baseplate forming an airtight seal.

Claim 29 is directed to a hybridization chamber comprising a base plate comprising a base cavity, a first array component in said base cavity, wherein the first array component comprises a plurality of assay locations, a lid comprising a plurality of first component ports, wherein each of the component ports comprises a second array component wherein said second array components align with corresponding assay locations of said first array component, a sealant between the base plate and the lid forming an airtight seal

Claim 40 is drawn to a hybridization chamber comprising a first array component comprising a plurality of assay locations, wherein the first array component is a multi-well plate, a lid comprising a plurality of second array components wherein a plurality of the second array components comprise an array comprising a plurality of different bioactive agents directly coupled to the second array component, wherein a plurality of the second array components are aligned with a corresponding well of the multi-well plate and at least one alignment feature configured to facilitate alignment of the lid with the first array component.

When rejecting claims under 35 U.S.C. §103, the Examiner bears the burden of establishing a *prima facie* case of obviousness. See, e.g., *In re Bell* 26 USPQ2d 1529 (Fed. Cir.

1993); M.P.E.P. Section 2142. To establish a *prima facie* case, three basic criteria must be met: (1) the prior art, either alone or in combination, must teach or suggest every limitation of the rejected claims; (2) the prior art must provide one of ordinary skill with a suggestion or motivation to modify or combine the teachings of the references relied upon by the Examiner to arrive at the claimed invention; and (3) the prior art must provide one of ordinary skill with a reasonable expectation of success.

The Examiner's position is that modifying the light-tight seal of Whitehead with the o-ring light-tight seal of Kolehmainen would be obvious to one of skill in the art for, as the Examiner noted, "the known and expected result of providing an alternative means recognized in the art to achieve the same result, sealing the interior of the reaction region from external light. Use of an o-ring as suggested by the reference of Kolehmainen et al. would inherently result in an airtight seal." Applicants respectfully traverse.

Initially, Applicants submit that replacement of an o-ring for a labyrinth joint in the device of Whitehead is not a replacement of alternative means recognized in the art to achieve the desired result. While it may be true that both the labyrinth joint and the o-ring result in a light-tight seal, an o-ring lacks several of the functional aspects of a labyrinth joint making the replacement of the o-ring for the labyrinth joint improper. Applicants submit that an o-ring can hardly be considered the equivalent of a joint as described and depicted in Whitehead.

In addition to providing a light-tight seal, the labyrinth joint provides a means for aligning or registering the lid **24** with the base **10**, of Whitehead. Having the labyrinth joint continue around the periphery of the housing (see column 4, line 66) ensures that the lid and base are properly engaged. Specifically, Whitehead asserts at column 5, lines 40-47

> The underside of the lower plate **24** is also provided with rectangular peripheral grooves **35** for receiving the ribs **21** of the housing **10** to provide a labyrinth joint between the support **23** and the housing **10**. The dimensions of the relevant components are such that, when the dispensing device is in position on the housing **10** (as illustrated in FIGS. 1 and 2), the lower ends of the tubes **28** project a short distance into the wells **16**.

In contrast, replacement of the labyrinth joint with the o-ring of Kolehmainen would compromise the alignment and registration of the tubes and wells due to the reduced structural rigidity of an o-ring. Thus, the replacement alleged in the Office Action would not adequately provide all of the desired functions of the Whitehead device. Furthermore, even if it were possible in hindsight to design a modification of the Whitehead device in which o-rings could functionally replace the labyrinth joint there is no teaching or suggestion in either of the references of how the elastic and pliable o-ring of Kolehmainen would provide any advantageous much less equivalent function as the labyrinth joint in aligning and registering the tubes and wells of Whiteheads device.

Applicants note that "[i]f proposed modification would render the prior art invention being modified unsatisfactory or its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir.

1984). Should the Examiner maintain this rejection, Applicants respectfully request evidence in support of the Examiner's position that an o-ring would have advantageous or even equivalent function as a labyrinth joint in providing alignment features as well as features of creating an air tight seal. *See M.P.E.P.* § 2144.03.

Applicants submit that "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990) (emphasis in original). Here, Applicants submit that despite the Examiner's characterization of the alleged motivation to replace the labyrinth joint of Whitehead with the o-ring of Kolehmainen, the suggestion to do so is not found in the cited references. Rather, the Examiner appears to be attempting at best a hindsight reconstruction of the invention using Applicants' specification as a template.

Moreover, in contrast to the Examiner's assertion, there is no teaching or suggestion in the cited references that simply replacing the labyrinth seal with an o-ring would result in an airtight seal. Applicants agree that under the right conditions and configuration, an o-ring can provide an airtight seal, as specifically outlined in Applicants' specification and currently claimed. However, there is no teaching or suggestion in the art of record of how to modify the device of Whitehead to form an airtight seal with an o-ring. Because an o-ring when used in the device of Whitehead would not necessarily result in an airtight seal, as claimed, Applicants

maintain that one skilled in the art would not have been motivated to make the claimed invention if presented with the combination of the Whitehead and Kolehmainen references.

Accordingly, Applicants respectfully submit that there is insufficient motivation for the combination of the references. Applicants respectfully request the Examiner to withdraw the rejection of claims 13, 29 and those claims that depend from them.

In addition, regarding claim 40, Applicants submit that neither Whitehead nor Kolehmainen teach each element of the claim. As noted previously, claim 40 sets forth, *inter alia,* "that a plurality of said second array components comprise an array comprising a plurality of different bioactive agents directly coupled to said second array component". However, neither Whitehead nor Kolehmainen teach or suggest that a plurality of the second array components comprise an *array* comprising a plurality of *different* bioactive agents directly coupled to the second array component.

In contrast, Whitehead discloses a "coated support array". *See* col,. 9, lines 40-45. However, there is no disclosure in Whitehead that a plurality of the "coated support arrays" include a plurality of *different* bioactive agents directly attached to a second array component. In addition, Kolehmainen fails to cure the deficiency of Whitehead. Kolehmainen fails to disclose direct attachment of bioactive agents to any array component. Accordingly, Applicants respectfully submit that the cited references fail to teach or suggest each element of claim 40. Accordingly, because there is inadequate motivation to combine the references and because the

references fail to teach each element of the claims, Applicants submit that a *prima facie* case of obviousness has not been established. Applicants respectfully request the Examiner to withdraw the rejection of claim 40 and those that depend from it.

Applicants note that claims 37-39 were not listed as being subject to this rejection at paragraph 8, p. 4 of the office action. However, at on p. 6 of the office action, the Examiner discusses them as though they were rejected along with clam 40. Thus, to the extent that these claims may be subject to this rejection under 35 USC 103, Applicants respectfully traverse.

Claim 37 recites that "said component ports comprise a second array component each second array component comprising a plurality of different bioactive agents". However, as noted previously, neither Whitehead nor Kolehmainen teach or suggest a plurality of said second array components comprise an array comprising a plurality of different bioactive agents. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

Claim 38 recites that "a plurality of said second array components comprise a plurality of different bioactive agents". However, as noted previously, neither Whitehead nor Kolehmainen teach or suggest a plurality of said second array components comprise an array comprising a plurality of different bioactive agents. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

Claim 39 recites that "a plurality of said second array components comprise a plurality of different bioactive agents". However, as noted previously, neither Whitehead nor Kolehmainen teach or suggest a plurality of said second array components comprise an array comprising a plurality of different bioactive agents. Accordingly, Applicants respectfully request the Examiner to withdraw this rejection.

B. Claims 36-51 are rejected under 35 U.S.C. 103 as being unpatentable over Whitehead in view of Kolehmainen taken further in view of Walt et al.

Kolehmainen and Whitehead are discussed above. Walt discloses bead-based sensors for detecting target analytes. In some embodiments beads are distributed in wells on the ends of fiber optic bundles.

The Examiner seems to have taken the position that the claims differ by "reciting that the second array component of the lid includes arrays of bioactive agents, specifically, a substrate that includes discrete sites containing microspheres of distinctive bioactive agents." The Examiner further notes that the reference of Whitehead discloses that the disclosed supports can take the form of fiber optic sensors and that it would have been obvious to one of ordinary skill in the art to employ the fiber optic sensor devices disclosed in Walt et al in the system of Whitehead et al for the known and expected result of providing a means recognized in the art for contacting a fiber optic sensor with a sample for analyte detection. Applicants respectfully traverse.

As noted previously, to establish a *prima facie* case, three basic criteria must be met: (1) the prior art, either alone or in combination, must teach or suggest every limitation of the rejected claims; (2) the prior art must provide one of ordinary skill with a suggestion or motivation to modify or combine the teachings of the references relied upon by the Examiner to arrive at the claimed invention; and (3) the prior art must provide one of ordinary skill with a reasonable expectation of success.

Claim 36 depends from claim 32, which ultimately depends from claim 29. Thus, the limitations of claim 29 also are included in claim 36. These include a hybridization chamber comprising a base plate comprising a base cavity, a first array component in said base cavity, wherein the first array component comprises a plurality of assay locations, a lid comprising a plurality of first component ports, wherein each of the component ports comprises a second array component wherein said second array components align with corresponding assay locations of said first array component, a sealant between the base plate and the lid forming an airtight seal.

For the reasons described above for claim 29, Applicants submit that there is inadequate motivation for the combination of the Whitehead and Kolehmainen. The response to the claim 29 rejection is incorporated herein by reference. In addition, Applicants submit that the teachings of Walt add little, if anything, to the discussion about replacing a labyrinth joint with an o-ring. For at least these reasons, Applicants submit that the rejection of claim 36 is improper. Applicants respectfully request the Examiner to withdraw the rejection of claim 36.

Likewise, claims 37, 38 and 39 all require a sealant between a base plate and a lid forming an airtight seal. For the reasons described above and incorporated herein by reference, Applicants submit that there is inadequate motivation for the combination of Whitehead with Kolehmainen. In addition, Applicants submit that the teachings of Walt add little, if anything, to the discussion about replacing a labyrinth joint with an o-ring. For at least these reasons, Applicants submit that the rejection of claim 37-39 is improper. Applicants respectfully request the Examiner to withdraw the rejection of claim 37-39 and those that depend from them.

Claim 40 is drawn to a hybridization chamber comprising a first array component comprising a plurality of assay locations, wherein the first array component is a multi-well plate, a lid comprising a plurality of second array components wherein a plurality of the second array components comprise an array comprising a plurality of different bioactive agents directly coupled to the second array component, wherein a plurality of the second array components are aligned with a corresponding well of the multi-well plate and at least one alignment feature configured to facilitate alignment of the lid with the first array component.

However, Applicants submit that the references alone or in combination fail to teach or suggest each element of the claims. As noted previously, neither Whitehead nor Kolehmainen teach or suggest that a plurality of the second array components comprise an array comprising a plurality of different bioactive agents directly coupled to the second array component.

In contrast, Whitehead discloses a "coated support array". *See* col,. 9, lines 40-45. The array has "downwardly extending supports 129...which have previously been coated with initiator, to dip into the liquid in the wells **16** to initiate the luminescence reaction." *See* col. 9, lines 42-46. However, there is no disclosure in Whitehead that any of the "coated support arrays" include a plurality of *different* bioactive agents. In addition, Kolehmainen fails to cure the deficiency of Whitehead. Kolehmainen fails to disclose direct attachment of bioactive agents to any array component. Walt discloses a plurality of different bioactive agents. However, as disclosed in Walt, bioactive agents are attached to microspheres, which are then distributed on a substrate such as a fiber optic bundle. However, the Examiner has failed to point to any disclosure in Walt of a plurality of different bioactive agents attached directly to a second array component. Accordingly, Applicants respectfully submit that the cited references fail to teach or suggest each element of claim 40. Accordingly, because there is inadequate motivation to combine the references and because the references fail to teach each element of the claims, Applicants submit that a *prima facie* case of obviousness has not been established. Applicants respectfully request the Examiner to withdraw the rejection of claim 40 and those that depend from it.

CONCLUSION

Applicants respectfully request that the rejections be withdrawn, and submit that the application is now in condition for allowance. Early notification of such is solicited. If, upon review, the Examiner feels there are additional outstanding issues, the Examiner is invited to call the undersigned.

Respectfully submitted,

DORSEY &WHITNEY LLP

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David C. Foster, Reg. No. 44,685
for
Robin M. Silva, Reg. No. 38,304
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Four Embarcadero Center
Suite 3400
San Francisco, CA 94111-4187
Telephone: (415) 781-1989